REMARKS

Applicant respectfully requests reconsideration. Claims 1, 4-9, 12, 13, 15-20, 22, 25-28, 129, 135-142 and 144-146 were previously pending in this application. No new matter has been added.

Double Patenting Rejection

Claims 1, 5-9, 12, 15-18, 22, 129, 135-137 and 139-142 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4, 5 and 9-14 of copending Application No. 10/300,247.

Applicant notes the provisional rejection but defers substantive rebuttal until the cited application is allowed. MPEP 804(I)(B) states that "the merits of such a provisional rejection *can* be addressed by both the applicant and the examiner without waiting for the first patent to issue" (emphasis added). Notably, the MPEP does not require that the merits *must* be addressed in such a situation. Moreover, the MPEP also states that "the 'provisional' double patent rejection should continue to be made by the examiner in each application as long as there are conflicting claims in more than one application unless that 'provisional' double patenting rejection is the only rejection remaining ...". Id. At that point, the examiner must withdraw the provisional rejection and allow the claims. Consistent with this practice, Applicant defers substantive rebuttal of the provisional rejections until the cited co-pending application is allowed.

Reconsideration and withdrawal of this rejection is respectfully requested.

Claims 1, 4-9, 12, 13, 15-20, 22, 25-28, 129, 135-142 and 144-146 are provisionally rejected on the ground of nonstatutory obviousness double patenting as being unpatentable over claims 1, 8-12, 20-33 and 35 of co-pending application 10/023,909 in view of Craig. The Examiner states that the rejected claims are obvious variants of the cited claims, although the latter do not recite inducing a mucosal immune response, because "the application specification discloses that the immune response encompasses a mucosal immune response (see p. 45)." The Examiner additionally cites Craig as reportedly teaching the use of "B-7 to upregulate the immune response to vaccines."

At the outset, Applicant notes that co-pending application 10/023,909 was allowed at the time the instant Office Action was mailed, and it issued on February 10, 2009. Thus the rejection is no longer provisional. Notwithstanding this, Applicant respectfully traverses for the reasons set forth below.

A nonstatutory double patenting rejection may be made between claims in an application and claims in a patent if such claims are not patentably distinct. Such a double patenting rejection requires (a) determination of (1) the scope and content of the patent claim relative to the rejected application claim, (2) the differences between the scope and content of the patent claim and the rejected application claim, and (3) the level of ordinary skill in the pertinent art, and (b) evaluation of objective indicia of non-obviousness. MPEP 804(II)(B)(1). Importantly, the comparison to be made is between the patent claim and the rejected application claim. The specification underlying the patent claim may be relied upon only in certain narrow instances (e.g., where the specification provides a definition of a patent claim term). To find obviousness type double patenting, the rejected application claim must be obvious in view of the patent claim, in the absence of the teachings in other references and typically in the absence of teachings from the underlying patent specification.

In view of the foregoing, the basis for the double patenting rejection is flawed. First, the Examiner's reliance on Craig is clearly improper. The rejected claims must be found to be obvious over the patent claims independent of Craig. Second, the Examiner's reliance on the teachings of the underlying patent specification is also improper at least because the cited passage does not teach what it is purported to teach. The Examiner has stated that the passage on page 45 of the co-pending application 10/023,909 as filed "discloses that the immune response encompasses a mucosal immune response." The passage does not provide such a teaching. Instead the passage refers to administration routes for an adjuvant combination that include mucosal as well as non-mucosal routes. The passage does not define terms in the cited patent claims. The Examiner's reliance on this passage is improper.

Notwithstanding this, the rejected application claims are not obvious variants of the cited patent claims at least because the differences between the two claim sets would not be obvious to one of ordinary skill in the art. For example, the rejected application claims all recite induction of a mucosal immune response in subjects in need of a mucosal immune response. These

limitations are not found in the patent claims nor are they obvious variants of such claims. Nothing in the patent claims leads one of ordinary skill in the art to the afore-mentioned limitations. The Examiner is apparently using hindsight by relying on teachings in the instant application. This too is improper.

Finally, MPEP 804(II) clearly states that double patenting is not to be confused with domination. Therefore to the extent that the Examiner may consider that the patent claims dominate, in whole or in part, the rejected application claims, this too is an improper basis for concluding that obviousness type double patenting exists.

For all of the foregoing reasons, a proper obviousness type double patenting rejection has not been made in view of the cited patent, and the rejected application claims are not obvious variants of the cited patent claims. Reconsideration and withdrawal are respectfully requested.

Rejection under 35 U.S.C. §103

Claims 1, 4-9, 12, 13, 15-20, 22, 25-28, 129, 135-142 and 144-146 are rejected under 35 U.S.C. §103(a) as being unpatentable over Krieg et al. (U.S. Patent No. 6,239,116) in view of each Agrawal et al. (U.S. Patent No. 6,426,334), Briles et al. (U.S. Patent No. 6,042,838), Craig (U.S. Patent No. 6,689,757), Kincy-Cain et al. (Infection and Immunity, 1996, 64:1437-1440) and Berzofsky et al. (U.S. Patent No. 6,749,856).

Applicant refers the Examiner to the previous rebuttal of this rejection. Here Applicant addresses the specific issues raised by the Examiner in the instant Office Action.

First, the Examiner cites Belyakov et al. PNAS 1998 95: 1709-1714 for the teaching that "mucosal vaccine(s) should encompass exogenous administration of IL-12 or a substance which stimulates IL-12 production." This argument however ignores the evidence of record that the role of IL-12 in mucosal immune responses was not clear at the time of filing. The Examiner is required to take into consideration the teachings of all of these references. MPEP 2143.01 (II).

As an example, Kincy-Cain et al. states that IL-12 can augment a mucosal immune response that arises after administration of intracellular pathogen *S. dublin*. However, the reference provides no data to evidence mucosal immune response induction, and instead infers mucosal immunity based on overall survival of the experimental subjects. The reference further

speculates that IL-12 "most probably" exerts its effects through non-antigen-specific mechanisms including through IFN-gamma production by innate immune cells such as NK cells.

Other references teach that IL-12 may not influence a mucosal immune response and/or that the role of IL-12 in this regard may vary depending on the route of administration. Some of these references indicate that mucosal immune responses occur even in the absence of IL-12. Simmons et al. (J. Immunol. 2002, 168:1804-1812) reports that IL-12 knockout (IL-12p40$^{-/-}$) mice mount gut-associated IgA responses after infection with *C. rodentium* (see for example Figure 6). The reference further reports that only a small fraction (10-15%) of the IL-12 knockout mice died post-infection, indicating that mice are able to clear the infection independent of IL-12. The reference concludes that gut-associated IgA responses are not defective in IL-12 deficient mice. Arulanandam et al. (Vaccine 1999, 17:252-260), published after Belyakov et al., states that "(T)here is little information about the influence of IL-12 on mucosal immunity." (See page 252, second column, second paragraph.) In support of this statement, the reference indicates that others have reported that intratracheal administration of IL-12 inhibits antigen-specific IgA in bronchoalveolar lavage (citing Yang et al. Nature Med. 1995 1:890-3) and that oral administration of IL-12 enhances serum IgG and has no effect on fecal IgA (citing Marinaro et al. J. Exp. Med. 1997 185:415-427). Arulanandam et al. itself reports no change in lung IgA levels and suppressed fecal IgA levels in mice immunized intranasally with DNP-OVA with cholera toxin B subunit and IL-12. The reference therefore shows that presence of IL-12 at a mucosal site does not induce mucosal IgA, and it further states that "only parenteral administration of IL-12 results in enhanced faecal IgA antibody levels." Marinaro et al. (J. Immunol. 1999, 162:114-121) documents that intranasal administration of IL-12 had no effect on mucosal secretory IgA responses to oral or nasal vaccines.

These reference teachings call into question the Examiner's reliance on only Belyakov et al. for the teaching that IL-12 (or agents that stimulate IL-12) should be used with mucosal vaccines. The Examiner is required to consider these reference teachings as a whole. MPEP 2143.01(II). Applicant submits that when the reference teachings are properly considered, the conclusion is that the role of (and thus the need for) IL-12 in mucosal immunity would not have been predictable to a person of ordinary skill in the art. Moreover, a person of ordinary skill in the art contemplating the use of IL-12 would not have known, been able to predict, or had a

reasonable expectation of success relating to whether a mucosal administration route would be suitable. In fact, the cited art suggests that, at least in some instances, a subject must be systemically exposed to IL-12 (e.g., via parenteral administration) rather than exposed at a mucosal surface.

Second, as argued previously, Craig teaches away from the rejected claims because Craig requires delivery of a nucleic acid that encodes an epitope (or antigen) while the rejected claims explicitly exclude such a limitation. The Examiner disregards this, and instead cites MPEP 2145 [R-6] XD for the proposition that "a teaching away from the invention is a teaching which renders prior art unsatisfactory for the intended purpose." Applicant assumes that the Examiner meant to cite MPEP 2145(X)(D) ("References Teach Away from the Invention or Render Prior Art Unsatisfactory for Intended Purpose" (emphasis added)) and will address the continued rejection on that assumption.

The Examiner has narrowly defined a teaching away as "a teaching that renders prior art unsatisfactory for the intended purpose." This is incorrect. A teaching away is more broadly defined by the MPEP and the courts to be a teaching that "leads away" from a claimed invention. MPEP 2141.02(VI). (See also Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc., 796 F.2d 443, 230 USPQ 416 (Fed. Cir. 1986) ("A reference should be considered as a whole, and portions arguing against or teaching away from the claimed invention must be considered."); Monarch Knitting Machinery Corp. V. Fukuhara Industrial & Trading Co., Ltd., 139 F.3d 977, 45 USPQ2d 1977 (Fed. Cir. 1998) ("A prior art reference may be considered to teach away when 'a person of ordinary skill, upon reading the reference, ... would be led in a direction divergent from the path that was taken by the applicant.'"). Thus, a teaching away includes a teaching that leads one of ordinary skill away from the claimed invention. A teaching away does not only exist where a teaching renders prior art unsatisfactory for its intended purpose, as suggested by the Examiner.

The instantly rejected claims all require that the antigen not be encoded in a nucleic acid vector. A necessary feature of Craig however is administration of a nucleic acid that encodes an epitope. Thus Craig is clearly directing the person of ordinary skill in a direction opposite to that of the rejected claims, and it is therefore teaching away from the claimed invention. The teaching in Craig discourages a common limitation of the rejected claims, and it is therefore

relevant to the issue of obviousness. In re Fulton, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004).

For at least these reasons, the combination of references does not render obvious the rejected claims. Reconsideration and withdrawal is respectfully requested.

CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, the Director is hereby authorized to charge any deficiency or credit any overpayment in the fees filed, asserted to be filed or which should have been filed herewith to our Deposit Account No. 23/2825, under Docket No. C1040.70006US00.

Respectfully submitted,

By 

Maria A. Trevisan
Registration No.: 48,207
WOLF, GREENFIELD & SACKS, P.C.
Federal Reserve Plaza
600 Atlantic Avenue
Boston, Massachusetts 02210-2206
617.646.8000

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